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Postoperative Stay Associated with Prognosis of Patients with Colorectal Cancer

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Objective

The author's objective was to determine whether the length of postoperative stay for patients after colorectal cancer surgery is associated with prognosis.

Summary Background Data

Financial pressure to reduce hospital costs has caused physicians to reduce hospital stays by changes in patient care, which reduce hospital stay but may compromise long-term results.

Methods

Using multivariate analysis, the author examined the relationship between postoperative stay and prognosis in a consecutive series of 341 prospectively studied patients with colorectal cancer undergoing potentially curative surgery.

Results

In multivariate analysis, patients staying beyond the median of 11 days had more complications ($p = 0.000$), more left hemicolectomies and procedures with colostomies ($p = 0.000$), were older ($p = 0.002$), and lost more blood ($p = 0.012$) than patients staying less than the median. Disease-free survival was significantly and independently related to Dukes' stage ($p = 0.000$), postoperative stay ($p = 0.001$), and blood transfusion ($p = 0.011$). The mean postoperative stay for the 98 patients who later developed recurrence was 15 days compared to 12 days for the 243 patients who remained disease free ($p = 0.0008$). Cumulative disease-free survival of the 142 patients who stayed more than the median of 11 days was 60% compared to 77% for the 199 patients with shorter stays ($p = 0.000$).

Conclusions

These data indicate that shorter hospital stays do not compromise disease-free survival of patients with colorectal cancer.

Dire predictions for the future well being of hospitalized patients accompanied the adoption of the diagnostic-related groups' prospective payment system. Physicians predicted that financial pressures on hospitals to reduce costs by shortening length of stay would cause patients to be discharged prematurely after surgery, contributing to increases in complications and, ultimately, mortality.[1] Physicians continue to cite third-party payers for pressure to reduce hospitalizations as being partly responsible when patients fair poorly after discharge or when managed without hospitalization. However, no published studies note increased rates of complications

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Table 1. COMPARISON OF SHORT AND LONG STAY PATIENTS

	Short Stay	Long Stay	p Value
N	199	142	
Age (yrs)	66	69	0.004
Admission hematocrit (%)	38.4	38.6	0.771
Discharge hematocrit (%)	34.5	33.8	0.107
Specimen length (cm)	30	29	0.488
Duration of surgery (min)	162	193	0.000
Blood loss (dL)	4.0	6.5	0.015
Tumor size (cc)	1855	1734	0.678
Blood transfused (units)	0.49	1.34	0.000

or mortality for any disease that could be related to early discharge or third-party refusal to hospitalize.

Hospital stay for a given surgical procedure is influenced by numerous variables, some of which are obvious and easy to measure[2,3] (*e.g.*, patient age, medical condition, and home environment) and some of which are subtle and difficult to evaluate[4] (*e.g.*, physician efficiency and operative techniques). In addition, the use and management of drains[5] and the rate of diet advancement[6] can profoundly influence length of stay. Hospital stays are shortening, in part because preoperative stays have been shortened or eliminated, patients go home with drains, and home care has been arranged. Subtle changes in physician behavior also can influence length of hospital stay. For example, high volume and participation in managed care plans are associated with shorter lengths of stay.[4] Our concern is that physicians may subtly change behavior in this cost-conscious environment, which may shorten length of stay at the expense of long-term good results. For example, one such subtle change in behavior potentially compromising long-term results would be less-extensive cancer surgery. If fewer lymph nodes are removed, involved lymph nodes may be missed and the extent of disease not appreciated. Potentially beneficial adjuvant therapy might not be given. If this is the case, as length of stay declines because surgery is less extensive, outcome for treatment of malignancies may deteriorate. This possibility was explored by studying the relationship between hospital stay for colorectal cancer surgery and disease-free survival. The possibility that factors influencing postoperative stay might influence survival was investigated.

MATERIALS AND METHODS

The study population was drawn from 484 consecutive patients scheduled for elective colorectal cancer surgery without evidence of liver or other metastases. These patients were identified before operation between August 1, 1983, and July 31, 1986, and 415 agreed to be observed annually. Despite preoperative criteria requiring that suspicion of liver or other metastases render patients ineligible for the study, 65 patients were found on surgical exploration to have liver metastases or unresectable local disease. Nine patients died of postoperative complications, leaving 341 for the study.

Information was recorded on age, sex, operative procedure, size of tumor, degree of differentiation, number of involved nodes, length of specimen, stage, admission and discharge hematocrits, duration of operation, transfusions, operative blood loss, and length of postoperative stay. Tumor differentiation was graded as well, moderate, or poor by the pathologists. Tumor size was calculated from the pathologists' measurements in the fresh state using the formula (length/2 X width/2 X pi). The pathologists also measured the length of each specimen in the fresh state.

Staging was by a modification of Dukes staging: A, limited to mucosa and submucosa; B1, infiltration of muscularis (nodes uninvolved); B2, infiltration of serosa (nodes uninvolved); C1, one to three involved nodes; and C2, more than three involved nodes.

Follow-up was obtained annually by direct letter or telephone contact with the patient whenever possible. Seven patients were lost to follow-up at 14, 19, 35, 45, 47, and 55 months. The data were analyzed separately, considering these patients to be disease free when lost and considering them to have recurred when lost. The significance of the observed differences was the same using both methods.

Patients were divided into two groups by the median postoperative stay, and the variables (*e.g.*, age, sex) of patients with prolonged postoperative stays (exceeding the median) were compared with the values of patients who did not have prolonged postoperative stays. Chi square and Student's t test were used where appropriate. The independent significance of variables affecting length of stay was evaluated using SAS BMDP stepwise logistic regression software[7] (Statistical Analysis Software Institute, Cary, NC) run on an IBM 370 computer (IBM), which is housed at the City University of New York Computing System. Cumulative 5-year disease-free survival was calculated using the life-table method of Cutler and Ederer.[8] Significance of the observed differences was evaluated by the Breslow test. Cox proportional hazards model was used to identify independently significant variables associated with disease-free survival.[9]

RESULTS

Postoperative Stay

The mean length of stay after surgery was 12.9 days and the median was 11 days. Forty-two percent (142) of the 341 patients had postoperative stays exceeding the

Table 2. DISTRIBUTION OF SHORT AND LONG STAY PATIENTS

	Short Stay (%)	Long Stay (%)	p Value
Sex			
Males	92 (53)	83 (47)	0.006
Females	107 (65)	59 (35)	
Operation			
Right hemicolectomy	50 (71)	20 (29)	
Transverse colectomy	6 (67)	3 (33)	
Left hemicolectomy	20 (48)	22 (52)	
Sigmoid resection	51 (73)	19 (27)	0.000
Anterior resection	53 (65)	28 (35)	
Anterior resection with colostomy	6 (19)	26 (81)	
Abdominoperineal resection	9 (29)	22 (71)	
Subtotal colectomy	4 (67)	2 (33)	
Differentiation			
Well	126 (59)	88 (41)	
Moderate	63 (59)	45 (41)	0.808
Poor	10 (53)	9 (47)	
Dukes' stage			
A	42 (65)	23 (35)	
B1	34 (63)	20 (37)	
B2	89 (55)	73 (45)	0.353
C1	26 (59)	18 (41)	
C2	8 (50)	8 (50)	
Complications			
No	188 (70)	80 (30)	0.000
Yes	11 (15)	62 (85)	
Transfusion			
No	153 (67)	77 (33)	0.000
Yes	46 (41)	65 (59)	

median of 11 days (Tables 1 and 2). In comparison with the patients with stays at or below the median, the long-stay patients were significantly older and more likely to be men. In addition, prolonged postoperative stays were associated with more complex procedures: long-stay patients had significantly more left colon resections and procedures with a colostomy, required an average of 29 more minutes to complete, lost more blood, received more transfusions, and developed more postoperative complications.

In multivariate analysis (in order of significance), complication, operative procedure, age, and operative blood loss were significantly and independently related to length of stay (Table 3). Sex, duration of surgery, and blood transfusion lost significance after consideration for complication, age, procedure, and blood loss.

Postoperative complications were the most significant factors contributing to postoperative stay. Eighty-five percent (62) of the 73 patients developing complications had prolonged stays compared to 30% (80) of the 268 patients without complications. The average length of stay for patients with complications was 20 days compared to 11 days for patients without complications ($p = 0.0001$).

The operative procedure was second to complication in significance for postoperative stay. The majority of patients undergoing a left hemicolectomy, anterior resection with colostomy, and abdominoperineal resection had long stays. The average length of stay for these patients was 16 days compared to 12 days for patients undergoing other procedures ($p = 0.0001$).

Age also was significantly and independently related to length of stay because the mean age of long-stay patients was 69 compared to 66 for short-stay patients. The mean postoperative stay for patients 70 and older was 14 days compared to 12 days for younger patients ($p = 0.0011$). Fifty-one percent of patients older than 70 had prolonged stays compared to 38% of younger patients ($p = 0.013$). The only additional factor significantly and independently related to length of stay was estimated blood loss. Sixty-three percent of patients with operative blood losses above the mean of 4.6 dL had prolonged stays compared to 33% of patients with less blood loss. Short-stay patients averaged 4.0 dL of blood loss compared to 6.5 dL for long-stay patients. Patients with blood loss above the mean of 4.6 dL stayed an average of 15 days after surgery compared to 12 days for patients with less blood loss ($p = 0.0001$).

Prognosis

Ninety-eight (30%) of the 341 patients are known to have recurred within 5 years of surgery (Table 4). Forty

Table 3. MULTIVARIATE ANALYSIS WITH POSTOPERATIVE STAY AS THE DEPENDENT VARIABLE

Variable	Chi Square	p Value
Age	9.65	0.002
Sex	4.92	0.027
Stage	1.14	0.339
Differentiation	1.17	0.326
Tumor size	0.54	0.465
Operative procedure	7.44	0.000
Operative blood loss	34.74	0.000
Transfusion	32.44	0.000
Duration of procedure	25.44	0.000
Admission hematocrit	0.03	0.860
Complication	78.83	0.000
Results of Stepwise Analysis		
Complication	68.88	0.000
Operative proceduure	44.09	0.000
Age	9.29	0.002
Operative blood loss	6.25	0.012

Table 4. COMPARISON OF PATIENTS WITH AND WITHOUT RECURRENCE

	Disease-Free	Recurred	p Value
N	243	98	
Age (yrs)	67	67	0.704
Admission hematocrit (%)	38.9	37.9	0.088
Discharge hematocrit (%)	34.5	33.4	0.023
Specimen length (cm)	29	27	0.305
Duration of surgery (min)	173	186	0.130
Blood loss (dL)	4.0	5.2	0.013
Tumor size (cc)	1779	1783	0.992
Blood transfused (units)	0.28	0.50	0.000
Postoperative stay (days)	12	15	0.000

initially recurred in the abdomen or pelvis, 38 developed liver metastases, 7 developed lung metastases, and 13 patients recurred in multiple sites simultaneously. Thirty-eight (11%) are known dead of other causes without recurrent colorectal cancer. Average follow-up of the remaining patients is 65 months.

Comparison of patients who recurred with those who remained disease free revealed significant differences (in order of significance) in Dukes stage, postoperative stay, blood transfusions, blood loss, complications, discharge hematocrit, and postoperative stay (Tables 4 and 5). Using multivariate analysis, after consideration for Dukes stage, only postoperative stay and blood transfusion continued to be statistically significant (Table 6). Forty-one percent of transfused patients developed a recurrence compared to 23% of untransfused patients. Five-year disease-free survival of transfused patients was 58% compared to 76% for patients not transfused ($p = 0.0001$).

Postoperative stay was significantly related to outcome because the mean postoperative stay for the 98 patients who later developed recurrences was 15 days compared to 12 days for the 243 patients who remained disease free ($p = 0.0008$). Forty-three (22%) of the 199 short-stay patients developed recurrences compared to 54 (38%) of the 142 patients who stayed more than 11 days. The disease-free survival of patients staying less than 12 days was 77% compared to 60% for patients staying more than 11 days ($p = 0.000$).

DISCUSSION

In this study, postoperative stay for patients with colorectal cancer was significantly related to complications, procedure, age, and blood loss. Disease-free survival was significantly related to Dukes stage, postoperative stay, and transfusion. Shorter postoperative stays were associated with better long-term survival. Patients staying the shortest intervals after surgery had the lowest risk of recurrence, whereas recurrence rates increased with increasing postoperative stay. The association of prognosis with postoperative stay could not be attributed to relationships between postoperative stay and other variables of potential prognostic importance.

In an overlapping group of patients, we previously showed that procedures with colostomies, age, complications, and receipt of blood transfusions were significantly and independently related to postoperative stay.[3] In the current analysis, we found that length of stay was inversely related to disease-free survival. However, stage was the most significant determinant of disease-free survival and not related to length of stay. In multivariate analysis after consideration for stage and postoperative stay, receipt of blood transfusions was the only remaining variable related to disease-free survival.

We and others have noted previously the association of blood transfusion with length of stay and prognosis.[3,10–12] Transfusion is associated with increased risk of infectious complications, which prolongs hospital stay, and transfusion has been identified as a marker of high-cost hospitalized patients as a result of their prolonged stays[13] and increased mortality.[14] However, transfusion also is associated with increased stay and with prognosis

Table 5. DISTRIBUTION OF PATIENTS WITH AND WITHOUT RECURRENCE

	Disease-Free (%)	Recurred (%)	p Value
Sex			
Males	118 (67)	57 (33)	0.098
Females	125 (64)	41 (36)	
Operation			
Right hemicolectomy	57 (70)	13 (30)	
Transverse colectomy	4 (67)	5 (33)	
Left hemicolectomy	27 (64)	15 (36)	
Sigmoid resection	49 (70)	21 (30)	0.095
Anterior resection	60 (74)	21 (26)	
Anterior resection with colostomy	21 (64)	11 (36)	
Abdominoperineal resection	19 (61)	12 (39)	
Subtotal colectomy	6 (100)	0 (0)	
Differentiation			
Well	149 (70)	65 (30)	
Moderate	79 (73)	29 (27)	0.806
Poor	15 (79)	4 (21)	
Dukes' stage			
A	65 (100)	0 (0)	
B1	43 (80)	11 (20)	
B2	105 (65)	57 (35)	0.000
C1	24 (55)	20 (45)	
C2	6 (38)	10 (62)	
Complications			
No	198 (75)	70 (25)	0.025
Yes	45 (62)	28 (38)	
Transfusion			
No	177 (77)	53 (23)	0.001
Yes	66 (59)	45 (41)	

Table 6. MULTIVARIATE ANALYSIS WITH DISEASE-FREE SURVIVAL AS THE DEPENDENT VARIABLE

Variable	Chi Square	p Value
Age	0.23	0.630
Sex	2.63	0.105
Stage	52.27	0.000
Differentiation	2.73	0.098
Tumor size	0.30	0.585
Operative procedure	0.83	0.362
Operative blood loss	6.99	0.008
Transfusion	13.46	0.000
Duration of procedure	2.61	0.106
Admission hematocrit	4.22	0.040
Postoperative stay	14.27	0.000
Complication	13.19	0.000
Results of Stepwise Analysis		
Stage	52.27	0.000
Postoperative stay	12.09	0.001
Transfusion	6.54	0.011

independent of complications. The association of transfusion with infectious complications and with prognosis has been attributed to immunosuppression, which has been shown to follow receipt of allogeneic blood in numerous clinical and experimental studies.[15]

Complications are major determinants of hospital stay after surgery of all types. McAleese and Olding-Snee studied 4018 consecutive patients admitted from 1988 to 1991, a period when length of stay declined from 9 to 6 days.[16] The average length of stay for patients with complications was three times that of uncomplicated cases. Stay for complicated cases declined as overall length of stay declined. They noted that 7 of 17 patients re-admitted for complications had been discharged earlier than the average length of stay for their condition. However, re-admission rates also declined as length of stay declined, whereas the complication rate was relatively constant. In a separate study of 1446 patients undergoing coronary artery bypass, hip replacement, cholecystectomy, or transurethral resection of the prostate, length of stay for patients with cholecystectomy was a significant predictor of re-admission: patients with longer lengths of stay were more likely to be re-admitted than patients with shorter lengths of stay.[17] This indicates that shorter lengths of stay are not necessarily linked to an increase in re-admissions. Their data and ours indicate that shortening stay may be reducing complications, leading to improvements in quality of care.

Complications and hospital stay tend to form a vicious cycle. Complications prolong postoperative stay and prolonged stays, particularly in the elderly, increase the risk of nosocomial infections, further prolonging hospital stay.[18] This suggests that postoperative stays should spiral down as complications are controlled. Greater emphasis on controlling complications should be rewarded with significant reductions in postoperative stay.

Why should postoperative stay be related to disease-free survival? A direct cause and effect mechanism seems unlikely. Rather, it is probable that long-stay patients had higher rates of recurrence because, in some subtle way, they were different than were short-stay patients; unmeasured variables contributed to disease recurrence, which also resulted in prolonged stay. There may have been subtle differences in disease stage not recognized by the Dukes system, or they may have been more immunosuppressed. Postoperative stay may reflect the combined weight of several prognostic variables that, when considered separately, are not significantly related to prognosis in the statistical sense, but when combined and reflected in postoperative stay become statistically significant.

This study was undertaken with the hypothesis that shorter hospital stays would lead to impaired survival after colorectal cancer surgery. Certainly, this hypothesis is rejected. The data indicate that patients with shorter postoperative stays have improved disease-free survival after consideration for stage of disease. The mechanism of this association is unknown, suggesting that systematic study of differences between long- and short-stay patients may identify additional prognostic factors associated with postoperative stay. Potentially, variables so identified may be manipulated in ways that reduce stay and improve disease-free survival.

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